Hematuria

recommended evaluation and indications for referral

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Objectives

- Define microscopic hematuria
- Describe the differences between glomerular and extraglomerular hematuria and the differences in management as a result
- Describe how other causes of hematuria can be diagnosed rapidly with simple urinalysis
- Describe indications for subspecialty referral

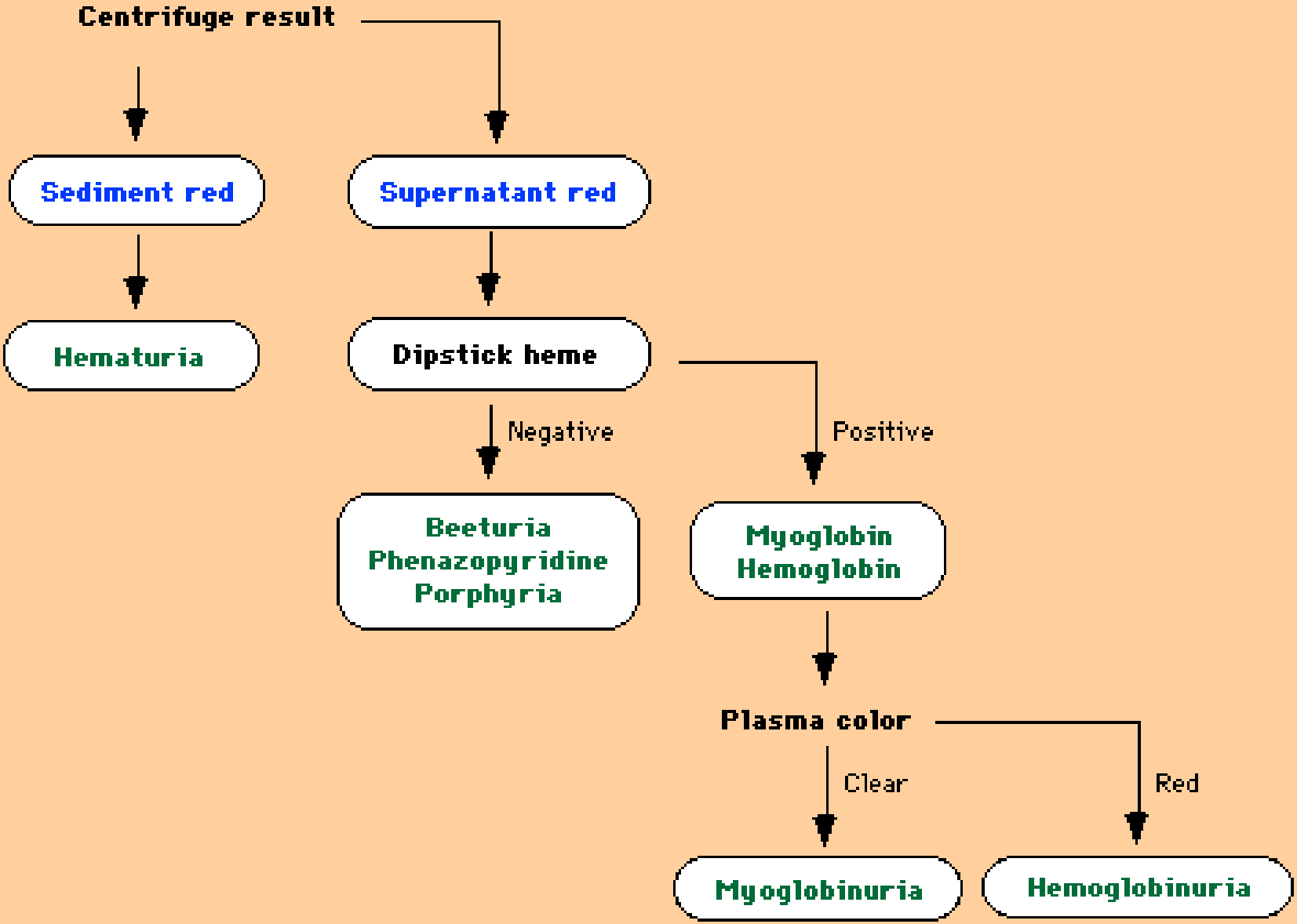
Definitions

- Macroscopic hematuria:
  - visible--urine is pink, red, or cola colored
- Microscopic
  - seen only under microscope
- Normally, 10^4 to 10^5 RBC's excreted in 12 hrs.
- Working definition: **>4 RBC's per high power field (HPF) of spun urine sediment**

Hematuria

- As little as 1 mL of blood per liter of urine can cause a visible color change
- Other conditions can color the urine
- Initial step is centrifuging urine to see if red color is in the sediment or the supernatant

Approach to the Patient with Red or Brown Urine

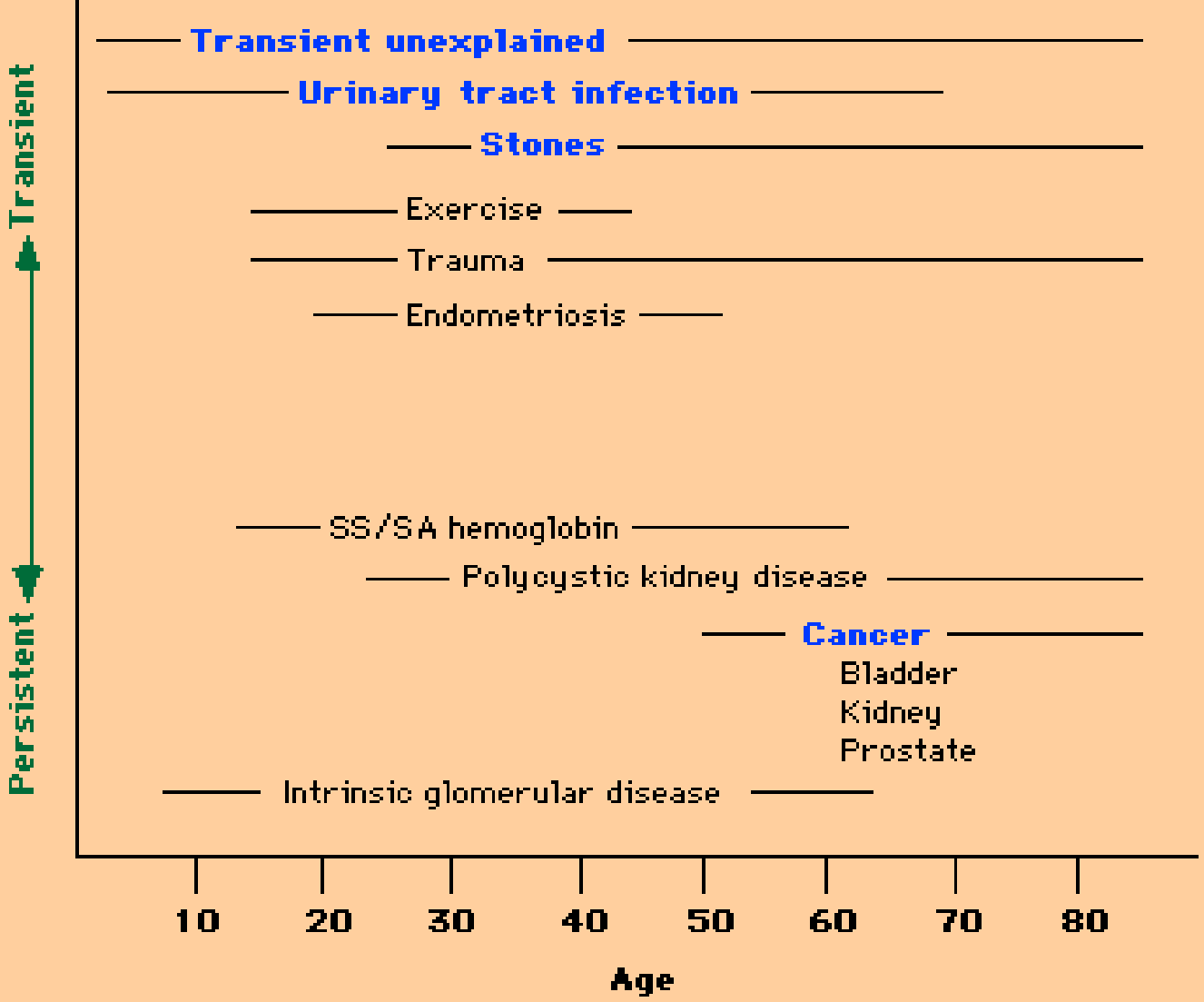


Hematuria

- Urine dipsticks for heme can detect 1-2 RBC's/HPF.
  - Are at least as sensitive as urine sediment but more likely to give false positives.
- Urine sediment exam is the gold standard--always use to confirm a positive dipstick

Hematuria

- Causes
  - See following figure
  - Most common are inflammation or infection of prostate or bladder
  - Kidney stones, malignancy, and glomerular diseases
  - BPH is a RARE cause of hematuria by itself



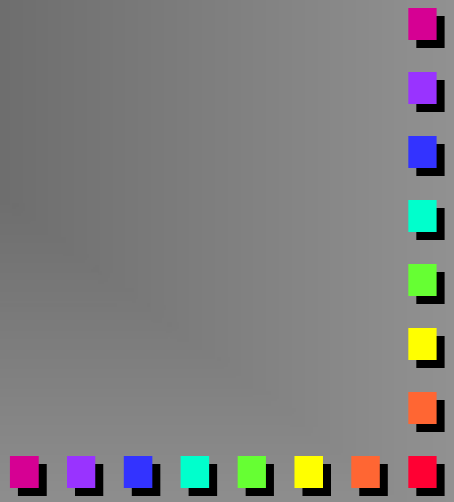
Major causes of hematuria by age and duration Schematic representations of the major causes of hematuria in relation to age at which they usually occur (horizontal axis), transience or persistence (vertical axis), and frequency (blue implies more frequent).

Initial evaluation of hematuria

- Is now considered primary care
- Addresses:
  - Any clues from history or physical suggesting a diagnosis?
  - Glomerular or extraglomerular bleeding?
  - Transient or persistent

Algorithm for hematuria

Hematuria algorithm



Historical clues

- Pyuria and dysuria--UTI
- Recent URI or skin infection (time frame for post-strep GN is 10-21 days, if earlier prob IgA nephropathy). Time frame following skin infection may be longer
- Positive family history of renal failure (hereditary nephritis or polycystic kidney disease)

Historical clues (cont’d)

- Unilateral flank pain, which may radiate to the groin--suggests ureteral obstruction due to blood clot or calculus. Can also be renal infarction. Rarely, if persistent can be loin pain hematuria
- Symptoms or prostatic obstruction
- Recent vigorous exercise or trauma.
- History or spontaneous bleeding disorder or bleeding from multiple sites on anticoagulation

Historical clues (cont'd)

- In contrast, warfarin therapy alone does not explain hematuria. Should be evaluated in the usual fashion unless bleeding from multiple sites with markedly abnormal coagulation studies.

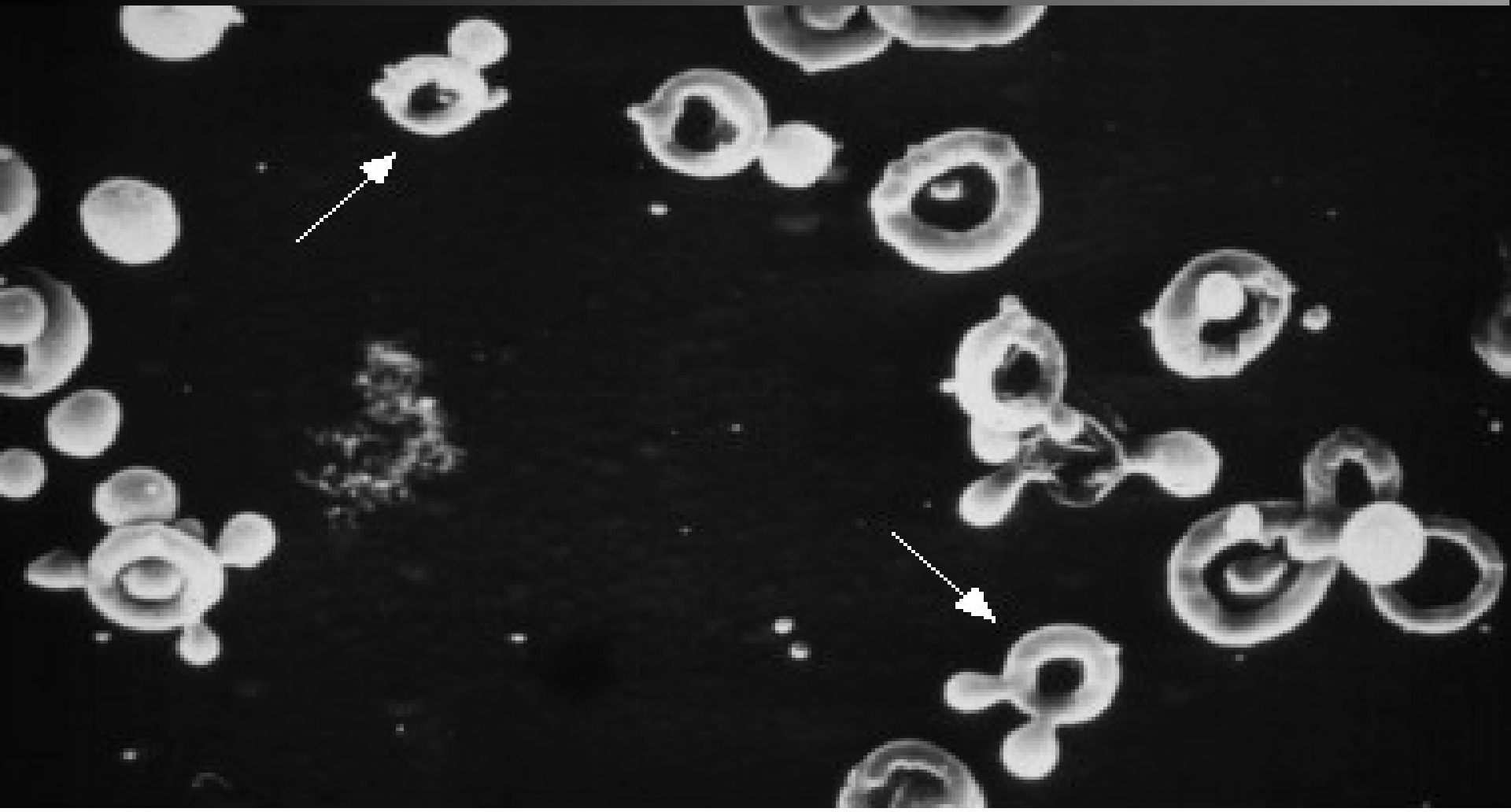
Historical clues (cont'd)

- Cyclic hematuria in women--suggests endometriosis of urinary tract. Contamination with menstrual blood is also possible.
- African American patients should be screened for sickle cell trait or disease

Glomerular vs. extraglomerular bleeding

- Patients with clear evidence of glomerular bleeding do not need urological evaluation at first--refer to nephrology first
- Signs:
  - RBC casts
  - Protein excretion>500 mg/d with no gross bleeding
  - Majority of cells with dysmorphic appearance
  - coca cola colored urine
  - hypertension
  - renal insufficiency

Click below to see University of Utah’s images of normal and abnormal red cells



Dysmorphic red cells Scanning microscopy showing dysmorphic red cells in a patient with glomerular bleeding. Acanthocytes can be recognized as ring forms with vesicle-shaped protrusions (arrows). Courtesy of Hans Köhler, MD.

Glomerular vs. extraglomerular bleeding

- Clots almost never occur in glomerular disease
- A three tube test may sometimes be useful:
  - The first few mL--urethral lesion
  - Mid-stream
  - the last few mL--lesion of bladder trigone
- Renal, ureteric, and diffuse bladder lesions give equal degrees of bleeding in all three samples

Glomerular vs. extraglomerular bleeding

- When persistent hematuria is the only manifestation of glomerular disease, most likely:
  - IgA nephropathy
  - Hereditary nephritis (positive family history of renal failure and often deafness)
  - Thin basement membrane disease (also called benign familial hematuria)--gross hematuria and family history of renal failure is unusual

Glomerular vs. extraglomerular bleeding

- Patients with glomerular hematuria should be referred to a nephrologist
  - More experienced at viewing urine sediment
  - Can decide on need for renal biopsy (generally not done for isolated hematuria)

Transient vs. persistent hematuria

- No cause of low-level hematuria, in the absence of other signs or symptoms, requires immediate diagnosis
- Reasonable to repeat UA in a few days
- Transient microscopic hematuria is a common problem in young adults. No obvious cause can be found in most cases.

Transient vs. persistent hematuria

- A very important EXCEPTION occurs in older patients
- Even transient hematuria has risk of malignancy.
- Neither cytology nor IVP reliably detected all tumors
- Ultrasound was good for renal tumors
- Cystoscopy was needed for bladder and prostate tumors

Transient vs. persistent hematuria

- Persistent hematuria in older adults (esp >50 yrs) mandates full evaluation

Radiologic tests

- Once glomerular bleeding excluded:
  - search for mass lesions in kidney, collecting system, ureters, and bladder
  - Diagnostic yield increases with age and is higher for gross hematuria (5-23%) than for microhematuria (14%) (See below)
  - If there is no specific clue, and IVP or renal ultrasound is reasonable. IVP is probably best test in young patients with normal renal function --can pick up lesions such as medullary sponge kidney not seen well on US.

Radiologic tests

- Young patients with a normal IVP don’t need US.
- Older patients are better served with US first, better at seeing small tumors. CT or MR is usually not required at first

Indications for cystoscopy

- When US or IVP is negative or incompletely defined.
- Yield of these procedures is low in men under 40 and in low risk women.
- Yield increase by risk factors of: age >50, phenacetin use, heavy smoking, exposure to aniline dyes, or longterm use of cyclophosphamide.

Followup

- About 1% of those with a negative initial exam will develop urinary tract malignancy within 3-4 years.
- Initial and periodic urinary cytology should be performed in high risk patients (eg, q 6 months).
- Some recommend repeat US and cysto at one year for high risk patients
- Low risk patients are followed with serial UA.

Unexplained hematuria

- Most common causes are
  - mild glomerular disease
  - Metabolic predisposition to stone disease (esp in young and middle-aged patients)
  - In pediatric population, 30-35% of idiopathic hematuria patients have hypercalciuria, 5-20% have hyperuricosuria (Both disorders often have family history) Hypocitruria less common
  - Dietary or medical therapy often resolves hematuria

Unexplained hematuria

- Hypercalciuria--
  - diet: reduce sodium intake (high sodium diet increases distal calcium delivery), avoidance of excessive protein intake (esp animal protein which has higher acid ash content), thiazide diuretics if needed
- Hyperuricosuria--
  - diet: low purine diet, allopurinol, occ potassium citrate

Unexplained hematuria

- Arteriovenous malformations and fistulas
  - May be congenital or acquired
  - Usu presents as gross hematuria
  - High output heart failure and hypertension may also occur
  - Suspect if irregular filling defect on IVP.
  - Confirmed by arteriography or fine cut CT (or MRA).
  - Can be ablated

Loin pain hematuria

- Loin or flank pain often severe and unrelenting with suggestion of glomerular hematuria.
  - Thin basement membrane disease may be an etiology
  - Psychological factors are significant--if no other cause found, treat as chronic pain syndrome (NSAID’s, TCA’s)

Screening for hematuria

- Not recommended in the absence of symptoms suggesting urinary tract disease
  - Little evidence it is a sensitive test for localized disease, or that early treatment of asymptomatic local disease results in better prognosis.

Exercise induced hematuria

- Trauma can’t be the only explanation since it can also occur after rowing and swimming
- Most cases are due to bladder sources but some are glomerular
- Renal ischemia may be responsible for these cases
- Regardless, it appears to be a benign condition if transient

Exercise induced hematuria

- Is a diagnosis of exclusion
  - Must be temporally related to exercise
  - Must remit within several days to at most one week
- Must be differentiated from myoglobinuria due to rhabdomyolysis and “march hemoglobinuria”--probable lysis of RBC’s as they pass through the dorsal vessels of the feet.